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EXAMINER
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BARTON, JEFFREY THOMAS

ART UNIT	PAPER NUMBER
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1753

DATE MAILED: 04/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

10/034,278

Applicant(s)

KURNIK ET AL.

Examiner

Jeffrey T. Barton

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 06 March 2006.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1,4-7 and 11-24 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,4-7 and 11-24 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 20060306.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 13 February 2006 has been entered.

### ***Response to Amendment***

2. The arguments filed on 13 February 2006 do not place the application in condition for allowance.

### ***Status of Rejections Pending Since the Office Action of 11 May 2005***

3. All previous rejections are maintained.

### ***Claim Rejections - 35 USC § 103***

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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5. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1, 4-7, and 14-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Manz et al in view of Křivánková et al.

Relevant to claim 1, Manz et al disclose a method for injecting a sample comprising a plurality of charged components and separating the components by electrophoresis in a microfluidic device (Column 1, lines 6-10; Column 2, lines 60-66), wherein said microfluidic device (Figures 1 and 3) includes a separation channel (22),

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having an upstream portion terminating in an upstream reservoir (R) and a downstream portion terminating in a downstream reservoir (W), sample and drain channels (23 and 24) intersecting the separation channel between the two channel portions at first and second junctions (25 and 26), respectively, and terminating in sample and drain reservoirs (S and D), respectively; and said device further includes electrodes in contact with the fluid in each said reservoir, including an upstream electrode, a downstream electrode, a sample electrode, and a drain electrode (Column 4, lines 4-10); the method comprising: a) placing into said separation channel, side channels and drain reservoir a first electrolyte solution (Column 3, line 66 - Column 4, line 3; Column 5, lines 35-38); b) placing into said sample reservoir the sample solution; c) creating a first voltage gradient between said sample electrode and said drain electrode, such that the charged components move into said separation channel (Column 5, lines 38-43), with the upstream and downstream electrodes being in a floating state during this step (Column 5, lines 43-47); and d) placing said sample and drain electrodes in a floating state, and creating a second voltage gradient between said downstream and upstream electrodes, such that the charged components move through the separation channel and separate into discrete bands according to their electrophoretic mobilities. (Column 5, lines 48-58; "switched off" would correspond to the definition of "floating" given at page 11, lines 15-19 of the applicants' specification)

Relevant to claims 4 and 5, Manz et al disclose the sample and drain channels intersecting the separation channels at either directly opposed junctions or at staggered junctions. (Column 4, lines 42-51)

Relevant to claim 6, Manz et al disclose the sample channel (23) being upstream of the drain channel (24). (Figure 3)

Manz et al do not explicitly disclose a method in which the sample solution and background electrolyte are chosen such that the first and second electrolyte solutions each comprise an ion having lower mobility in an electric field than any of said charged components, and one or the other of said electrolyte solutions comprises an ion having higher mobility in an electric field than any of said charged components, nor do they explicitly disclose the injection step including sample stacking within a region of said separation channel. (Claim 1)

Relevant to claim 1, Křivánková et al disclose a method of sample stacking in capillary electrophoresis (Section 5, Sample induced transient ITP in CZE; further discussion on pages 31-33) in which the sample solution and background electrolyte are chosen such that the first (background) and second (sample) electrolyte solutions each comprise an ion having lower mobility in an electric field than any of said charged components (B in figure 24), and one or the other of said electrolyte solutions comprises an ion having higher mobility in an electric field than any of said charged components (A in figure 24), which is present in a higher concentration than said charged components. (e.g. Figure 23 (b) and (c); 100-300 mM NaCl with 0.1 mM sample) The stacking occurs due to isotachophoresis (Transient ITP; Section 5), and will result in increased sample concentration (i.e. "into a small volume"), as shown in Figure 23 and discussed

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in the paragraph bridging the 1<sup>st</sup> and 2<sup>nd</sup> columns of page 29 - "sharp peaks" indicates a narrow sample band, with a corresponding smaller volume.

Relevant to claims 14 and 15, Křivánková et al disclose within their method the use of negatively charged sample components and chloride as the higher mobility ion (Figure 23)

Relevant to claim 16, Křivánková et al disclose the use of imidazole as the low-mobility ion with negatively charged analytes. (Table 3)

Relevant to claims 17 and 18, Křivánková et al disclose the low-mobility ion having a concentration of 10 mM in a separation. (Figure 23)

Relevant to claims 19 and 20, Křivánková et al disclose analysis of charged sample components having a concentration of 0.1  $\mu$ M. (Figure 21)

Relevant to claims 21 and 22, Křivánková et al disclose the high-mobility ion having a concentration of 3-20 mM (Table 2), and also show experiments where its concentration ranges from 0-300 mM. (Figure 23)

Relevant to claim 23, Křivánková et al disclose a method in which only the first (i.e. leading) electrolyte solution comprises the high mobility ion. (Figure 18) This leading electrolyte also served as the background electrolyte for capillary zone electrophoresis.

Relevant to claim 24, Křivánková et al disclose a method in which only the second (i.e. sample) electrolyte solution comprises the high mobility ion. (Section 5)

Addressing claim 1, it would have been obvious to one having ordinary skill in that art at the time the invention was made to modify the method of Manz et al by using samples and electrolytes that would provide sample stacking upon injection and electric field application, as taught by Křivánková et al, because Křivánková et al teach the advantages of using such isotachophoretic stacking methods in capillary electrophoresis methods, in that it allows increased sensitivity and analysis speed. (Conclusions) The use of electrokinetic injection as described in the method of Manz with such a sample as described by Křivánková et al would lead to a degree of isotachophoretic sample stacking within the separation channel in the injection step. (i.e. step (c) of the instant claim)

Addressing claim 7, it would also be obvious to use the downstream side channel as the sample source, and the upstream side channel as the drain, because it would be equally effective in transferring sample into the separation channel, and in the case of positively charged analytes, it would facilitate sample stacking in the appropriate direction. (i.e. the direction of the electric field in the separation channel during injection would be the same as that during separation)

Addressing claims 14-24, examples of electrolytes and suitable concentrations from Křivánková et al, referenced to instant claims, are given above. Any would be obvious to use in a combined method.

8. Claims 1, 4-7, and 14-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shultz-Lockyear et al in view of Křivánková et al.



Relevant to claim 1, Shultz-Lockyear et al disclose a method for injecting a sample comprising a plurality of charged components and separating the components by electrophoresis in a microfluidic device (Figure 3 and caption), wherein said microfluidic device (Figure 1) includes a separation channel having an upstream portion terminating in an upstream reservoir (3) and a downstream portion terminating in a downstream reservoir (4), sample and drain channels (connecting reservoirs 1 and 2 to the separation channel) intersecting the separation channel between the two channel portions at first and second junctions, respectively, and terminating in sample and drain reservoirs (1 and 2), respectively; and said device further includes electrodes in contact with the fluid in each said reservoir, including an upstream electrode, a downstream electrode, a sample electrode, and a drain electrode (Section 3.3 describes voltage application, electrodes are inherently present in each reservoir); the method comprising:

- a) placing into said separation channel, side channels and drain reservoir a first electrolyte solution (Section 3.1 describes buffer; for device to operate the channels must have been filled);
- b) placing into said sample reservoir the sample solution;
- c) creating a first voltage gradient between said sample electrode and said drain electrode, such that the charged components move into said separation channel (See Figure 3 and caption), with the upstream and downstream electrodes being in a floating state during this step (Figure 3 caption);
- and d) placing said sample and drain electrodes in a floating state, and creating a second voltage gradient between said downstream and upstream electrodes, such that the charged components move through the separation

channel and separate into discrete bands according to their electrophoretic mobilities.

(Figure 3 caption)

Also relevant to claim 1, Shultz-Lockyear et al disclose sample stacking within their device with certain buffer and sample choices. (Figure 7 and discussion)

Relevant to claim 5, Shultz-Lockyear et al disclose the sample and drain channels intersecting the separation channels with staggered junctions. (Figures 1 and 3)

Relevant to claim 7; Shultz-Lockyear et al disclose the sample channel (Connected to reservoir 1) being downstream of the drain channel (Connected to reservoir 2). (Figure 3)

Shultz-Lockyear et al do not explicitly disclose a method in which the sample solution and background electrolyte are chosen such that the first and second electrolyte solutions each comprise an ion having lower mobility in an electric field than any of said charged components, and one or the other of said electrolyte solutions comprises an ion having higher mobility in an electric field than any of said charged components, nor do they explicitly disclose the injection step including sample stacking within a region of said separation channel.

The disclosure of Křivánková et al is as described above in paragraph 7.

It would have been obvious to one having ordinary skill in that art at the time the invention was made to modify the method of Shultz-Lockyear et al by using samples and electrolytes that would provide sample stacking upon injection and electric field application, as taught by Křivánková et al, because Křivánková et al teach the advantages of using such isotachophoretic stacking methods in capillary electrophoresis methods, in that it allows increased sensitivity and analysis speed (Conclusions), and Shultz-Lockyear teach that such stacking occurs in their system with certain buffer/sample combinations. (Figure 7 and its description) The use of electrokinetic injection as described in the method of Shultz-Lockyear et al with such a sample as described by Křivánková et al would lead to a degree of isotachophoretic sample stacking within the separation channel in the injection step. (i.e. step (c) of the instant claim)

Regarding claim 4, Shultz-Lockyear et al disclose how their disclosed double-T injector allows for very small sample plugs. (Abstract; 1<sup>st</sup> sentence) It would certainly have been obvious to one having ordinary skill in the art to place the side channels directly opposite each other in the case that the smallest sample plug possible were desired. Such geometries are entirely conventional in the microfluidic art.

Regarding claim 6, it would also be obvious to use the upstream side channel as the sample source, and the downstream side channel as the drain, because it would be equally effective in transferring sample into the separation channel, and in the case of negatively charged analytes, it would facilitate sample stacking in the appropriate

direction. (i.e. the direction of the electric field in the separation channel during injection would be the same as that during separation)

Regarding claims 14-24, examples of electrolytes and suitable concentrations from Křivánková et al, referenced to instant claims, are given above in paragraph 7. Any would be obvious to use in a combined method.

9. Claims 11 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Manz et al and Křivánková et al as applied to claim 1 above, and further in view of Ramsey. (US 6,342,142)

Manz et al and Křivánková et al disclose a combined method as described above in addressing claim 1.

Neither Manz et al nor Křivánková et al explicitly disclose a method wherein the charged components are selected from the group consisting of nucleic acids, proteins, polypeptides, polysaccharides, and synthetic polymers (Claim 11); or a method of claim 11 wherein said charged components comprise nucleic acids. (Claim 12)

Ramsey discloses a method wherein the sample comprises nucleic acids. (Column 20, lines 35-36)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to use the combined method of Manz et al and Křivánková et al to analyze samples comprising nucleic acids, because such capillary electrophoretic methods provide excellent resolution of mixtures of charged molecules. (See Manz et al, Background and Summary sections; numerous cited examples in Křivánková et al)

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Furthermore, it would have been within the level of ordinary skill in the electrophoresis art to select a suitable analyte from materials (such as nucleic acids) which were well known as being separable by electrophoretic methods.

10. Claims 11 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shultz-Lockyear et al and Křivánková et al as applied to claim 1 above, and further in view of Ramsey. (US 6,342,142)

The reasoning for this rejection parallels that given above in paragraph 9.

11. Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Manz et al and Křivánková et al as applied to claim 1 above, and further in view of Fuchs et al.

Manz et al and Křivánková et al describe a combined method as described above in addressing claim 1.

Neither Manz et al nor Křivánková et al explicitly describe analysis of a sample as claimed in claim 13.

Fuchs et al disclose an electrophoretic method wherein the charged components of the sample comprise labeled molecules having distinct and characterized electrophoretic mobilities (Column 23, lines 29-53; Column 26, lines 19-53), said molecules having been cleaved from molecular species with biological or chemical recognition properties in the course of a multiplexed chemical or biochemical assay (Column 23, line 29 - Column 24, line 47)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to further modify the method of Manz et al by analyzing a sample as taught by Fuchs et al, because Fuchs et al demonstrate the desirability of electrophoretic analysis of such mixtures, and selection of any particular known type of sample for analysis would have been well within the level of ordinary skill in the art.

12. Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Shultz-Lockyear et al and Křivánková et al as applied to claim 1 above, and further in view of Fuchs et al.

The reasoning for this rejection parallels that given in paragraph 11 above.

13. Claims 1 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fuchs et al in view of Křivánková et al and either Manz et al or Shultz-Lockyear.

Fuchs et al disclose a method for injecting a sample comprising a plurality of charged components and separating the components by electrophoresis in a microfluidic device (Column 4, lines 24-38), wherein said microfluidic device (Figures 1a and 1b) includes a separation channel (20), having an upstream portion terminating in an upstream reservoir and a downstream portion terminating in a downstream reservoir (Both reservoirs labeled 16), sample and drain channels intersecting the separation channel between the two channel portions at first and second junctions, respectively, and terminating in sample and drain reservoirs (24 and 26), respectively; and said device further includes electrodes in contact with the fluid in each said reservoir

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(Column 20, lines 61-63), including an upstream electrode, a downstream electrode, a sample electrode, and a drain electrode; the method comprising: a) placing into said separation channel, side channels and drain reservoir a first electrolyte solution (Column 20, lines 53-56; necessary for electrokinetic motion); b) placing into said sample reservoir the sample solution (Column 20, lines 56-59); c) creating a first voltage gradient between said sample electrode and said drain electrode (Column 15, lines 52-62; Column 20, lines 56-63), such that the charged components move into said separation channel; and d) creating a second voltage gradient between said downstream and upstream electrodes, such that the charged components move through the separation channel and separate into discrete bands according to their electrophoretic mobilities. (Column 16, lines 15-52)

Also relevant to claim 1, Fuchs et al disclose isotachophoretic concentration of a sample within their electrophoresis method. (Column 23, lines 48-53)

Relevant to claim 13, Fuchs et al disclose a method wherein the charged components comprise labeled molecules having distinct and characterized electrophoretic mobilities (Column 23, lines 29-53; Column 26, lines 19-53), said molecules having been cleaved from molecular species with biological or chemical recognition properties in the course of a multiplexed chemical or biochemical assay (Column 23, line 29 - Column 24, line 47)

Fuchs et al do not explicitly disclose a method in which the sample solution and background electrolyte are chosen such that the first and second electrolyte solutions

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each comprise an ion having lower mobility in an electric field than any of said charged components, and one or the other of said electrolyte solutions comprises an ion having higher mobility in an electric field and higher concentration than any of said charged components, nor do they explicitly disclose the injection step including sample stacking within a region of said separation channel.

Fuchs et al also do not explicitly disclose placing the upstream and downstream electrodes in a floating state during the injection step or placing said sample and drain electrodes in a floating state concurrently with application of the potential between upstream and downstream electrodes.

Křivánková et al disclose a method of sample stacking in capillary electrophoresis (Section 5, Sample induced transient ITP in CZE; further discussion on pages 31-33) in which the sample solution and background electrolyte are chosen such that the first (background) and second (sample) electrolyte solutions each comprise an ion having lower mobility in an electric field than any of said charged components (B in figure 24), and one or the other of said electrolyte solutions comprises an ion having higher mobility in an electric field than any of said charged components (A in figure 24), which is present in a higher concentration than said charged components. (e.g. Figure 23 (b) and (c); 100-300 mM NaCl with 0.1 mM sample) The stacking occurs due to isotachophoresis (Transient ITP; Section 5), and will result in increased sample concentration (i.e. "into a small volume"), as shown in Figure 23 and discussed in the



paragraph bridging the 1<sup>st</sup> and 2<sup>nd</sup> columns of page 29 - "sharp peaks" indicates a narrow sample band, with a corresponding smaller volume.

Manz et al disclose a similar microfluidic device in which they carry out an injection method comprising the steps of placing the upstream and downstream electrodes in a floating state while applying a voltage to inject a sample (Column 5, lines 43-46), and placing said sample and drain electrodes in a floating state concurrently with application of the potential between upstream and downstream electrodes. (Column 5, lines 48-58)

Shultz-Lockyear et al disclose a similar microfluidic device in which they carry out an injection method comprising the steps of placing the upstream and downstream electrodes in a floating state while applying a voltage to inject a sample, and placing said sample and drain electrodes in a floating state concurrently with application of the potential between upstream and downstream electrodes. (Figure 3 and caption)

It would have been obvious to one having ordinary skill in that art at the time the invention was made to modify the method of Fuchs et al by using samples and electrolytes that would provide sample stacking upon injection and electric field application, as taught by Křivánková et al, because it requires a simpler electrolyte system than typical isotachophoretic methods, Fuchs et al described using isotachophoretic stacking within their method (Column 23, lines 48-53), and Křivánková et al teach the advantages of using such isotachophoretic stacking methods in capillary

electrophoresis methods, in that it allows increased sensitivity and analysis speed.

(Conclusions) Furthermore, the use of electrokinetic injection would lead to a degree of sample stacking within the separation channel in the injection step. (i.e. step (c) of the instant claim)

It would also have been obvious to allow the electrodes in the upstream and downstream reservoirs to float during injection and to allow the electrodes in the sample and waste reservoirs to float after injection, as taught by either Manz et al or Shultz-Lockyear et al, because it provides the simplest method of injection and separation. (i.e. only applying a potential to two electrodes at a time) Furthermore, since Fuchs is silent concerning the specifics of the injection procedure, a skilled artisan would look to the teaching of other prior art methods (e.g. Manz et al, Shultz-Lockyear et al) for suitable methods. As these references teach the effectiveness of their injection methods, it would have been obvious to use them.

### ***Response to Arguments***

14. Applicant's arguments filed 13 February 2006 have been fully considered but they are not fully persuasive.

Regarding one portion of the motivation to combine Manz et al with Křivánková et al, Applicant argues that there is in fact no suggestion by Manz et al to perform sample stacking, as discussed in the interview and clearly argued in the remarks submitted on 13 February 2006. These arguments are convincing, and the Examiner has removed this basis of motivation from the rejections above. However, there is still clear

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suggestion by Křivánková et al that these stacking techniques are highly advantageous in capillary electrophoresis, and the combination is still considered valid based on this motivation, regardless of the differences in the respective systems pointed out by Applicant in the remarks. Anyone of ordinary skill in the art would have recognized that use of samples and buffers as described by Křivánková et al in the system of Manz et al would have resulted in successful stacking.

Regarding the claim of “unsuggested benefits” on page 10 of the remarks, in no way does this overcome a rejection under 35 U.S.C. §103. There is nothing unexpected in the “better peak sharpness and intensity” described by Applicant, and no demonstration that any purported superiority is a result of the claimed method, as opposed to sample choice, column length, or any other property of the system.

Regarding Fuchs et al, Applicant argues that Fuchs does not disclose ITP in a separation method. This is simply not true. The cited section clearly teaches, “separating the detectable complex formed from any unreacted labeled detectable binding partner using capillary electrophoresis”, the isotachophoretic method is then cited as a preferred method of concentrating the sample. (Column 23, lines 39-53) In any event, the motivation provided by the teaching of Křivánková et al is not addressed by these arguments.

### ***Conclusion***

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Jeffrey Barton, whose telephone number is (571)


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272-1307. The examiner can normally be reached Monday-Friday from 9:00 am – 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nam Nguyen, can be reached at (571) 272-1342. The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free).

JTB  
26 April 2006

  
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